

19 JAN 2005

## PCT REQUEST

UCL-044-PCT

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0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using <b>PCT-EASY Version 2.92 (updated 01.01.2003)</b>	
0-5	<b>Petition</b> The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant) <b>European Patent Office (EPO) (RO/EP)</b>	
0-7	Applicant's or agent's file reference <b>UCL-044-PCT</b>	
I	Title of invention <b>METHOD FOR THE SYNTHESIS OF ANTHRACYCLINE-PEPTIDE CONJUGATES</b>	
II	<b>Applicant</b>	
II-1	This person is: <b>applicant only</b>	
II-2	Applicant for <b>all designated States except US</b>	
II-4	Name <b>UNIVERSITE CATHOLIQUE DE LOUVAIN</b>	
II-5	Address: <b>Place de l'Université 1 B-1348 Louvain-La-Neuve Belgium</b>	
II-6	State of nationality <b>BE</b>	
II-7	State of residence <b>BE</b>	
II-8	Telephone No. <b>+32 10 47 24 97</b>	
II-9	Facsimile No. <b>+32 10 47 48 30</b>	
III-1	<b>Applicant and/or inventor</b>	
III-1-1	This person is: <b>applicant only</b>	
III-1-2	Applicant for <b>all designated States except US</b>	
III-1-4	Name <b>DIATOS S.A.</b>	
III-1-5	Address: <b>166, boulevard de Montparnasse F-75014 Paris France</b>	
III-1-6	State of nationality <b>FR</b>	
III-1-7	State of residence <b>FR</b>	

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III-2	Applicant and/or inventor	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	FERNANDEZ, Anne-Marie
III-2-5	Address:	16, avenue des Lucanes B-1070 Bruxelles Belgium
III-2-6	State of nationality	FR
III-2-7	State of residence	BE
III-3	Applicant and/or inventor	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	DUBOIS, Vincent
III-3-5	Address:	Rue de Wangenies 124 B-6220 Fleurus Belgium
III-3-6	State of nationality	BE
III-3-7	State of residence	BE
IV-1	Agent or common representative; or address for correspondence  The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: Name (LAST, First)	agent
IV-1-1	Address:	BRANTS, Johan, Philippe, Emile
IV-1-2		De Clercq, Brants & Partners E. Gevaertdreef 10a B-9830 Sint-Martens-Latem Belgium
IV-1-3	Telephone No.	+32 9 280 23 40
IV-1-4	Facsimile No.	+32 9 280 23 45
IV-1-5	e-mail	info@dcbpatent.com
IV-2	Additional agent(s)	additional agent(s) with same address as first named agent
IV-2-1	Name(s)	DE CLERCQ, Ann

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V	<b>Designation of States</b>	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	<p>AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT</p> <p>EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT</p> <p>EP: AT BE BG CH&amp;LI CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT SE SI SK TR and any other State which is a Contracting State of the European Patent Convention and of the PCT</p> <p>OA: BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT</p>
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	<p>AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&amp;LI CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW</p>
V-5	<b>Precautionary Designation Statement</b>  In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	<b>Exclusion(s) from precautionary designations</b>	NONE
VI-1	<b>Priority claim of earlier regional application</b>	
VI-1-1	Filing date	24 July 2002 (24.07.2002)
VI-1-2	Number	02447145.0
VI-1-3	Regional Office	EP

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VI-2	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1	
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)	
VII-2	Request to use results of earlier search; reference to that search		
VII-2-1	Date	24 July 2002 (24.07.2002)	
VII-2-2	Number	02447145.0	
VII-2-3	Country (or regional Office)	EP	
VIII	Declarations	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	
IX	Check list	number of sheets	electronic file(s) attached
IX-1	Request (including declaration sheets)	5	-
IX-2	Description	28	-
IX-3	Claims	6	-
IX-4	Abstract	1	EZABST00.TXT
IX-5	Drawings	0	-
IX-7	TOTAL	40	
IX-8	Accompanying items	paper document(s) attached	electronic file(s) attached
IX-17	Fee calculation sheet	✓	-
IX-17	PCT-EASY diskette	-	Diskette
IX-19	Figure of the drawings which should accompany the abstract		
IX-20	Language of filing of the international application	English	
X-1	Signature of applicant, agent or common representative		
X-1-1	Name (LAST, First)	BRANTS, Johan, Philippe, Emile	

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10-1	Date of actual receipt of the purported international application	
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10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

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11-1	Date of receipt of the record copy by the International Bureau	
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## PCT (ANNEX - FEE CALCULATION SHEET)

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(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only		
0-1	International Application No.		
0-2	Date stamp of the receiving Office		
0-4	Form - PCT/RO/101 (Annex) PCT Fee Calculation Sheet Prepared using		
0-4-1	PCT-EASY Version 2.92 (updated 01.01.2003)		
0-9	Applicant's or agent's file reference		
2	Applicant		
12	UNIVERSITE CATHOLIQUE DE LOUVAIN, et al.		
12-1	Calculation of prescribed fees	fee amount/multiplier	Total amounts (EUR)
12-2-1	Transmittal fee	T	⇒ 100
12-2-2	Search fee	S	⇒ 945
12-3	International search to be carried out by	EP	
12-4	International fee		
	Basic fee (first 30 sheets)	b1	444
12-4	Remaining sheets		10
12-5	Additional amount	(X)	10
12-6	Total additional amount	b2	100
12-7	b1 + b2 =	B	544
12-8	Designation fees		
12-9	Number of designations contained in international application		95
12-10	Number of designation fees payable (maximum 5)		5
12-11	Amount of designation fee	(X)	96
12-12	Total designation fees	D	480
12-13	PCT-EASY fee reduction	R	-137
12-14	Total International fee (B+D-R)	I	⇒ 887
12-15	Fee for priority document		
12-16	Number of priority documents requested		1
12-17	Fee per document	(X)	30
12-18	Total priority document fee	P	⇒ 30
12-19	<b>TOTAL FEES PAYABLE (T+S+I+P)</b>		⇒ 1,962
	Mode of payment		

## VALIDATION LOG AND REMARKS

## PCT (ANNEX - FEE CALCULATION SHEET)

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13-2-7	Validation messages Contents	Yellow! The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.
		Green? The international application contains no drawings. Please verify.
13-2-8	Validation messages Fees	Green? Please confirm that fee schedule utilized is the latest available
13-2-9	Validation messages Payment	Yellow The Payment page has not been completed.

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**PCT-EASY INFORMATION SHEET**  
(For applicant use only, DO NOT submit this sheet with the international application)

**VALIDATION LOG**

Yellow!	<b>Contents</b> The power of attorney or a copy of the general power of attorney will need to be furnished unless all applicants sign the request form.
Green?	The international application contains no drawings. Please verify.
Green?	<b>Fees</b> Please confirm that fee schedule utilized is the latest available
Yellow	<b>Payment</b> The Payment page has not been completed.

Before submitting the International Application, please carefully verify that:

- the information contained on printed Request form is correct;
- Box X of the Request form has been signed;
- all elements of the International application as indicated in Boxes VIII and IX of the Request form have been attached; and,
- the diskette containing the PCT-EASY zip file of the International Application has been enclosed and has been clearly labeled "PCT-EASY", with the applicant's or agent's file reference, and the first applicant's name.

**ATTENTION**

DO NOT modify any indications on the Request form printout. The electronic version of the PCT-EASY application has been locked. If an error or an omission is discovered at this time, you must reopen the stored form for submission, perform necessary amendments and immediately resubmit the form. Finally, a NEW submission diskette must be created manually by resending the corrected stored form to the diskette. The previously created printout and submission diskette must be destroyed in order to prevent the possibility of erroneously sending it to the RO.

The present invention relates to a method for the preparation of a compound of formula (I) or pharmaceutical acceptable salts thereof and intermediates thereof, comprising the steps of:

- a) halogenating a compound of formula (II), resulting in compound of formula (IIa),
- b) reacting a compound of formula (IIa) at its 14 position with the thiol moiety of a peptide of formula (III), in the presence of a suitable linker, to obtain said compound of formula (I),

wherein R1 represents OH, NH<sub>2</sub> or NH-peptide; R2 represents H or -CO-peptide; R3 represents OCH<sub>3</sub>, OH R4 represents H, or COCF<sub>3</sub>; R5 represents OH, O-tetrahydropyranyl or H; R6 represents OH or H; R7 represents H, OH, OCO(CH<sub>2</sub>)<sub>3</sub>CH<sub>3</sub> or OCOCH(OC<sub>2</sub>H<sub>5</sub>)<sub>2</sub>; R8 represents OH or H; R9 represents OH or H; R10 represents a halogen and L is an optional suitable linker arm.

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